

## SEQUENCE LISTING

<110> Oostra, Ben Heutink, P Duijin, C.M.  
<120> DIAGNOSTICS AND THERAPEUTICS FOR AUTOSOMAL DOMINANT  
HEMOCHROMATOSIS  
<130> 24584  
<150> 60/301,429  
<151> 2001-06-29  
<160> 4  
<170> PatentIn version 3.1  
<210> 1  
<211> 2443  
<212> DNA  
<213> Homo sapiens  
<220>  
<221> mutation  
<222> (733)..(735)  
<223>  

|   |     |
|---|-----|
| <400> 1   | 60  |
| agctggctca gggcgtccgc taggctcgga cgacctgctg agcctccaa accgcttcca        | 120 |
| taaggcttg ctttccaaact tcagctacag tggtagtaa gtttggaaag aaggaaaaaa        | 180 |
| gaaaatccct gggccctt tcttttgc tttgccaag tcgtcggtgt agtcttttg             | 240 |
| cccaaggctg ttgtgtttt agaggtgtca tctccaggtc cttgcactcc tgtaacaag         | 300 |
| cacctcagc agagcagcag cagcgatage agccgcagaag gagccagcg ggtcgcttag        | 360 |
| tgtcatgacc agggcgggag atcacaaacc ccagagagga tgctgtggat cttggccgaa       | 420 |
| ctacctgacc tctgc当地aaat tccttc当地ta ctttgc当地at tcttc当地ta cttggggaga       | 480 |
| tcggatgtgg cactttggc tggatgtggat tctggtagag ctctatggaa acagccctct       | 540 |
| tttgc当地ga agtctacgggc tggatgtggat agggatgtggat ctggatgtggat gagccatcat  | 600 |
| cggtgactgg gtggacaaga atgctagact taaatggcc cagacccgc tggatgtggat        | 660 |
| aatgtttca gtc当地ccctgt gtggatcat cttgtatgtat gtttcttac ataaatcatgt       | 720 |
| rcttc当地acc tggatgtggat gatggatgtggat cacttc当地gc tataatccgtat tcatcactat | 780 |
| tgcaatatttgc acatgtttgg ccaatgtttgg tactgtatgtat gtttcttac ataaatcatgt  |     |

|             |              |             |             |              |             |      |
|-------------|--------------|-------------|-------------|--------------|-------------|------|
| tgttgtgtt   | gcaggagaag   | acagaagcaa  | actagcaaat  | atgaatgcc    | caatacagaag | 840  |
| gattgaccag  | ttaaccaaca   | tcttagcccc  | catggctgtt  | ggccagatta   | tgacattttg  | 900  |
| ctccccagtc  | atcggtgtg    | gctttatcc   | ggatggaa    | ttgttatcca   | tgtcgctgga  | 960  |
| gtacgtctg   | ctctggaaagg  | tttacagaa   | aacccagct   | ctagctgtg    | aagctggct   | 1020 |
| taaagaagag  | gaaactgaat   | tgaacacgct  | gaatttacac  | aaagatact    | agccaaaacc  | 1080 |
| cctggaggga  | actcatctaa   | tgggtgtgaa  | ggactctaa   | atccatgac    | ttgaacatg   | 1140 |
| gcaagagcct  | acttgtgcct   | cccagatggc  | tgagcccttc  | cgtaccccttcc | gagatggatg  | 1200 |
| ggtgtcttac  | tacaaccaggc  | ctgtgtttct  | ggctggcatg  | ggcttgcgtt   | tcctttat    | 1260 |
| gactgtctg   | ggctttgact   | gcatcaccac  | agggtacgccc | tacactcagg   | gactgatgg   | 1320 |
| ttccatcttc  | agtatttga    | tgggagatc   | agctataact  | ggaataatgg   | qaactgtagc  | 1380 |
| ttttacttgg  | ctacgtcgaa   | aatgtgtt    | ggtctggaca  | ggtctgatct   | caggattggc  | 1440 |
| acagctttcc  | tggttgcattct | tgtgtgtat   | ctctgtattc  | atgcgtggaa   | gcccccttgg  | 1500 |
| cttgcgtt    | tctcccttttgc | aagatatccg  | atcaagggtt  | atcaaggag    | agtcaattac  | 1560 |
| acatccaag   | atacctgaaa   | ttacaactga  | aatatacatg  | tctaatgggt   | ctaatctgc   | 1620 |
| taatattgtc  | ccggagacaa   | gtcctgtatc  | tgtgcccata  | atctctgtca   | gtctgtgtt   | 1680 |
| tgccaggcgtc | attgtctgtca  | gaatcggtct  | ttggcccttt  | gatthaactg   | tgacacagtt  | 1740 |
| gctgcaagaa  | aatgtattg    | aatctgaaa   | aggcattata  | aatgtgtac    | agaactccat  | 1800 |
| gaactatctt  | cttgatcttc   | tgcatcttcat | catggtcatc  | ctggctccaa   | atctgtggc   | 1860 |
| ttttgggttgc | ctcgatattga  | tttcagtc    | ctttgtggca  | atggccacaa   | ttatgtat    | 1920 |
| ccgatttgc   | caaaaacttc   | tggaaacaa   | gtctttgt    | tgccgtctg    | atgcaaaaga  | 1980 |
| agtaggaag   | gaaaatcaag   | caaatacatc  | tgtgtttga   | gacatgttta   | ctgtgtctat  | 2040 |
| cctgttacta  | gattatata    | agcacatgt   | cttattttgt  | actgcagaat   | tccaaaat    | 2100 |
| ggctgggtgt  | tttgcgtt     | tttaccaca   | gtctgtcc    | gagaactaa    | agctgtttag  | 2160 |
| gaaacctaag  | tcagcagaaa   | ttaactgatt  | aattccctt   | atgttgaggc   | atggaaaaaa  | 2220 |
| aatggaaaa   | aggaaaaact   | cagtttaaa   | tacggagac   | tataatggat   | aacactgrat  | 2280 |
| tcccttattt  | ctcatgat     | gatacaatct  | tacgtaaa    | agtgtttagt   | cacgtgtaa   | 2340 |
| cagttatcat  | ttgacagatt   | cttacatgt   | ctagaattca  | gatatgtcg    | ttttctgc    | 2400 |
| aactactct   | tgttcaagac   | tagctaa     | attttttgc   | atc          |             | 2443 |

9923514-101001  
<211> 571

<212> PRT

<213> Homo sapiens

<400> 2

Met Thr Arg Ala Gly Asp His Asn Arg Gln Arg Gly Cys Cys Gly Ser  
1 5 10 15

Leu Ala Asp Tyr Leu Thr Ser Ala Lys Phe Leu Leu Tyr Leu Gly His  
20 25 30

Ser Leu Ser Thr Trp Gly Asp Arg Met Trp His Phe Ala Val Ser Val  
35 40 45

Phe Leu Val Glu Leu Tyr Gly Asn Ser Leu Leu Leu Thr Ala Val Tyr  
50 55 60

Gly Leu Val Val Ala Gly Ser Val Leu Val Leu Gly Ala Ile Ile Gly  
65 70 75 80

Asp Trp Val Asp Lys Asn Ala Arg Leu Lys Val Ala Gln Thr Ser Leu  
85 90 95

Val Val Gln Asn Val Ser Val Ile Leu Cys Gly Ile Ile Leu Met Met  
100 105 110

Val Phe Leu His Lys His Glu Leu Leu Thr Met Tyr His Gly Trp Val  
115 120 125

Leu Thr Ser Cys Tyr Ile Leu Ile Ile Thr Ile Ala Asn Ile Ala Asp  
130 135 140

Leu Ala Ser Thr Ala Thr Ile Ile Gln Arg Asp Trp Ile Val  
145 150 155 160

Val Val Ala Gly Glu Asp Arg Ser Lys Leu Ala Asn Met Asn Ala Thr  
165 170 175

Ile Arg Arg Ile Asp Gln Leu Thr Asn Ile Leu Ala Pro Met Ala Val  
180 185 190

Gly Gln Ile Met Thr Phe Gly Ser Pro Val Ile Gly Cys Gly Phe Ile  
195 200 205

Ser Gly Trp Asn Leu Val Ser Met Cys Val Glu Tyr Val Leu Leu Trp  
210 215 220

Lys Val Tyr Gln Lys Thr Pro Ala Leu Ala Val Lys Ala Gly Leu Lys  
225 230 235 240

Glu Glu Glu Thr Glu Leu Lys Gln Leu Asn Leu His Lys Asp Thr Glu  
245 250 255

Pro Lys Pro Leu Glu Gly Thr His Leu Met Gly Val Lys Asp Ser Asn  
260 265 270

Ile His Glu Leu Glu His Glu Gln Glu Pro Thr Cys Ala Ser Gln Met  
275 280 285

Ala Glu Pro Phe Arg Thr Phe Arg Asp Gly Trp Val Ser Tyr Tyr Asn  
290 295 300

Gln Pro Val Phe Leu Ala Gly Met Gly Leu Ala Phe Leu Tyr Met Thr  
305 310 315 320

Val Leu Gly Phe Asp Cys Ile Thr Thr Gly Tyr Ala Tyr Thr Gln Gly  
325 330 335

Leu Ser Gly Ser Ile Leu Ser Ile Leu Met Gly Ala Ser Ala Ile Thr  
340 345 350

Gly Ile Met Gly Thr Val Ala Phe Thr Trp Leu Arg Arg Lys Cys Gly  
355 360 365

Leu Val Arg Thr Gly Leu Ile Ser Gly Leu Ala Gln Leu Ser Cys Leu  
370 375 380

Ile Leu Cys Val Ile Ser Val Phe Met Pro Gly Ser Pro Leu Asp Leu  
385 390 395 400

Ser Val Ser Pro Phe Glu Asp Ile Arg Ser Arg Phe Ile Gln Gly Glu  
405 410 415

Ser Ile Thr Pro Thr Lys Ile Pro Glu Ile Thr Thr Glu Ile Tyr Met  
420 425 430

Ser Asn Gly Ser Asn Ser Ala Asn Ile Val Pro Glu Thr Ser Pro Glu  
435 440 445

Ser Val Pro Ile Ile Ser Val Ser Leu Leu Phe Ala Gly Val Ile Ala

450

455

460

Ala Arg Ile Gly Leu Trp Ser Phe Asp Leu Thr Val Thr Gln Leu Leu  
465 470 475 480

Gln Glu Asn Val Ile Glu Ser Glu Arg Gly Ile Ile Asn Gly Val Gln  
485 490 495

Asn Ser Met Asn Tyr Leu Leu Asp Leu Leu His Phe Ile Met Val Ile  
500 505 510

Leu Ala Pro Asn Pro Glu Ala Phe Gly Leu Leu Val Leu Ile Ser Val  
515 520 525

Ser Phe Val Ala Met Gly His Ile Met Tyr Phe Arg Phe Ala Gln Asn  
530 535 540

Thr Leu Gly Asn Lys Leu Phe Ala Cys Gly Pro Asp Ala Lys Glu Val  
545 550 555 560

Arg Lys Glu Asn Gln Ala Asn Thr Ser Val Val  
565 570

<210> 3

<211> 571

<212> PRT

<213> Homo sapiens

<220>

<221> VARIANT

<222> 144

<223>

<400> 3

Met Thr Arg Ala Gly Asp His Asn Arg Gln Arg Gly Cys Cys Gly Ser  
1 5 10 15

Leu Ala Asp Tyr Leu Thr Ser Ala Lys Phe Leu Leu Tyr Leu Gly His  
20 25 30

Ser Leu Ser Thr Trp Gly Asp Arg Met Trp His Phe Ala Val Ser Val  
35 40 45

100-7388-1010000

Phe Leu Val Glu Leu Tyr Gly Asn Ser Leu Leu Leu Thr Ala Val Tyr  
50 55 60

Gly Leu Val Val Ala Gly Ser Val Leu Val Leu Gly Ala Ile Ile Gly  
65 70 75 80

Asp Trp Val Asp Lys Asn Ala Arg Leu Lys Val Ala Gln Thr Ser Leu  
85 90 95

Val Val Gln Asn Val Ser Val Ile Leu Cys Gly Ile Ile Leu Met Met  
100 105 110

Val Phe Leu His Lys His Glu Leu Leu Thr Met Tyr His Gly Trp Val  
115 120 125

Leu Thr Ser Cys Tyr Ile Leu Ile Ile Thr Ile Ala Asn Ile Ala His  
130 135 140

Leu Ala Ser Thr Ala Thr Ala Ile Thr Ile Gln Arg Asp Trp Ile Val  
145 150 155 160

Val Val Ala Gly Glu Asp Arg Ser Lys Leu Ala Asn Met Asn Ala Thr  
165 170 175

Ile Arg Arg Ile Asp Gln Leu Thr Asn Ile Leu Ala Pro Met Ala Val  
180 185 190

Gly Gln Ile Met Thr Phe Gly Ser Pro Val Ile Gly Cys Gly Phe Ile  
195 200 205

Ser Gly Trp Asn Leu Val Ser Met Cys Val Glu Tyr Val Leu Leu Trp  
210 215 220

Lys Val Tyr Gln Lys Thr Pro Ala Leu Ala Val Lys Ala Gly Leu Lys  
225 230 235 240

Glu Glu Glu Thr Glu Leu Lys Gln Leu Asn Leu His Lys Asp Thr Glu  
245 250 255

Pro Lys Pro Leu Glu Gly Thr His Leu Met Gly Val Lys Asp Ser Asn  
260 265 270

Ile His Glu Leu Glu His Glu Gln Glu Pro Thr Cys Ala Ser Gln Met  
275 280 285

Ala Glu Pro Phe Arg Thr Phe Arg Asp Gly Trp Val Ser Tyr Tyr Asn  
290 295 300

Gln Pro Val Phe Leu Ala Gly Met Gly Leu Ala Phe Leu Tyr Met Thr  
305 310 315 320

Val Leu Gly Phe Asp Cys Ile Thr Thr Gly Tyr Ala Tyr Thr Gln Gly  
325 330 335

Leu Ser Gly Ser Ile Leu Ser Ile Leu Met Gly Ala Ser Ala Ile Thr  
340 345 350

Gly Ile Met Gly Thr Val Ala Phe Thr Trp Leu Arg Arg Lys Cys Gly  
355 360 365

Leu Val Arg Thr Gly Leu Ile Ser Gly Leu Ala Gln Leu Ser Cys Leu  
370 375 380

Ile Leu Cys Val Ile Ser Val Phe Met Pro Gly Ser Pro Leu Asp Leu  
385 390 395 400

Ser Val Ser Pro Phe Glu Asp Ile Arg Ser Arg Phe Ile Gln Gly Glu  
405 410 415

Ser Ile Thr Pro Thr Lys Ile Pro Glu Ile Thr Thr Glu Ile Tyr Met  
420 425 430

Ser Asn Gly Ser Asn Ser Ala Asn Ile Val Pro Glu Thr Ser Pro Glu  
435 440 445

Ser Val Pro Ile Ile Ser Val Ser Leu Leu Phe Ala Gly Val Ile Ala  
450 455 460

Ala Arg Ile Gly Leu Trp Ser Phe Asp Leu Thr Val Thr Gln Leu Leu  
465 470 475 480

Gln Glu Asn Val Ile Glu Ser Glu Arg Gly Ile Ile Asn Gly Val Gln  
485 490 495

Asn Ser Met Asn Tyr Leu Leu Asp Leu Leu His Phe Ile Met Val Ile  
500 505 510

Leu Ala Pro Asn Pro Glu Ala Phe Gly Leu Leu Val Leu Ile Ser Val  
515 520 525

Ser Phe Val Ala Met Gly His Ile Met Tyr Phe Arg Phe Ala Gln Asn

530

535

540

Thr Leu Gly Asn Lys Leu Phe Ala Cys Gly Pro Asp Ala Lys Glu Val  
545 550 555 560

Arg Lys Glu Asn Gln Ala Asn Thr Ser Val Val  
565 570

<210> 4

<211> 571

<212> PRT

<213> Homo sapiens

<220>

<221> misc\_feature

<222> 144

<223> Xaa = any amino acid except Asp

<400> 4

Met Thr Arg Ala Gly Asp His Asn Arg Gln Arg Gly Cys Cys Gly Ser  
1 5 10 15

Leu Ala Asp Tyr Leu Thr Ser Ala Lys Phe Leu Leu Tyr Leu Gly His  
20 25 30

Ser Leu Ser Thr Trp Gly Asp Arg Met Trp His Phe Ala Val Ser Val  
35 40 45

Phe Leu Val Glu Leu Tyr Gly Asn Ser Leu Leu Leu Thr Ala Val Tyr  
50 55 60

Gly Leu Val Val Ala Gly Ser Val Leu Val Leu Gly Ala Ile Ile Gly  
65 70 75 80

Asp Trp Val Asp Lys Asn Ala Arg Leu Lys Val Ala Gln Thr Ser Leu  
85 90 95

Val Val Gln Asn Val Ser Val Ile Leu Cys Gly Ile Ile Leu Met Met  
100 105 110

TRANSLATION

Val Phe Leu His Lys His Glu Leu Leu Thr Met Tyr His Gly Trp Val  
115 120 125

Leu Thr Ser Cys Tyr Ile Leu Ile Ile Thr Ile Ala Asn Ile Ala Xaa  
130 135 140

Leu Ala Ser Thr Ala Thr Ala Ile Thr Ile Gln Arg Asp Trp Ile Val  
145 150 155 160

Val Val Ala Gly Glu Asp Arg Ser Lys Leu Ala Asn Met Asn Ala Thr  
165 170 175

Ile Arg Arg Ile Asp Gln Leu Thr Asn Ile Leu Ala Pro Met Ala Val  
180 185 190

Gly Gln Ile Met Thr Phe Gly Ser Pro Val Ile Gly Cys Gly Phe Ile  
195 200 205

Ser Gly Trp Asn Leu Val Ser Met Cys Val Glu Tyr Val Leu Leu Trp  
210 215 220

Lys Val Tyr Gln Lys Thr Pro Ala Leu Ala Val Lys Ala Gly Leu Lys  
225 230 235 240

Glu Glu Glu Thr Glu Leu Lys Gln Leu Asn Leu His Lys Asp Thr Glu  
245 250 255

Pro Lys Pro Leu Glu Gly Thr His Leu Met Gly Val Lys Asp Ser Asn  
260 265 270

Ile His Glu Leu Glu His Glu Gln Glu Pro Thr Cys Ala Ser Gln Met  
275 280 285

Ala Glu Pro Phe Arg Thr Phe Arg Asp Gly Trp Val Ser Tyr Tyr Asn  
290 295 300

Gln Pro Val Phe Leu Ala Gly Met Gly Leu Ala Phe Leu Tyr Met Thr  
305 310 315 320

Val Leu Gly Phe Asp Cys Ile Thr Thr Gly Tyr Ala Tyr Thr Gln Gly  
325 330 335

Leu Ser Gly Ser Ile Leu Ser Ile Leu Met Gly Ala Ser Ala Ile Thr  
340 345 350

Gly Ile Met Gly Thr Val Ala Phe Thr Trp Leu Arg Arg Lys Cys Gly

355

360

365

Leu Val Arg Thr Gly Leu Ile Ser Gly Leu Ala Gln Leu Ser Cys Leu  
370 375 380

Ile Leu Cys Val Ile Ser Val Phe Met Pro Gly Ser Pro Leu Asp Leu  
385 390 395 400

Ser Val Ser Pro Phe Glu Asp Ile Arg Ser Arg Phe Ile Gln Gly Glu  
405 410 415

Ser Ile Thr Pro Thr Lys Ile Pro Glu Ile Thr Thr Glu Ile Tyr Met  
420 425 430

Ser Asn Gly Ser Asn Ser Ala Asn Ile Val Pro Glu Thr Ser Pro Glu  
435 440 445

Ser Val Pro Ile Ile Ser Val Ser Leu Leu Phe Ala Gly Val Ile Ala  
450 455 460

Ala Arg Ile Gly Leu Trp Ser Phe Asp Leu Thr Val Thr Gln Leu Leu  
465 470 475 480

Gln Glu Asn Val Ile Glu Ser Glu Arg Gly Ile Ile Asn Gly Val Gln  
485 490 495

Asn Ser Met Asn Tyr Leu Leu Asp Leu Leu His Phe Ile Met Val Ile  
500 505 510

Leu Ala Pro Asn Pro Glu Ala Phe Gly Leu Leu Val Leu Ile Ser Val  
515 520 525

Ser Phe Val Ala Met Gly His Ile Met Tyr Phe Arg Phe Ala Gln Asn  
530 535 540

Thr Leu Gly Asn Lys Leu Phe Ala Cys Gly Pro Asp Ala Lys Glu Val  
545 550 555 560

Arg Lys Glu Asn Gln Ala Asn Thr Ser Val Val  
565 570